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## Effects of respiratory rehabilitation for patients with novel coronavirus (COVID-19) pneumonia in the rehabilitation phase: Protocol for a systematic review and meta-analysis

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**Effects of respiratory rehabilitation for patients with novel coronavirus  
(COVID-19) pneumonia in the rehabilitation phase: Protocol for a  
systematic review and meta-analysis**

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23 **ABSTRACT**

24 **Introduction:** Recent viral pneumonia infected by Coronavirus Disease 2019  
25 (COVID-19) has attracted the attention of people all over the world. We aim to  
26 investigate the effects of respiratory rehabilitation therapy on patients with novel  
27 coronavirus by conducting this systematic review and meta-analysis.

28 **Methods and analysis:** Ethics approval is not required because this is a  
29 protocol for a systematic review and meta-analysis. This systematic review and  
30 meta-analysis has been registered in the PROSPERO. The PubMed, Embase,  
31 Web of Science, the Cochrane Central Register of Controlled Trials  
32 (CENTRAL), Chinese Biomedical Literature Database (CBM), China National  
33 Knowledge Infrastructure (CNKI), Wanfang and VIP information databases will  
34 be searched from their inception time to April 15, 2020 without restricting  
35 research types to find relevant studies. Two reviewers will independently extract  
36 data and perform quality assessment of included studies. Review Manager 5.3  
37 software (Cochrane Collaboration) and Stata 16.0 software will be used to  
38 conduct this meta-analysis. Mean difference (MD) or standardized mean  
39 difference (SMD) with 95% confidence intervals (CI) is used for calculating  
40 continuous variables to synthesize data.

41 **Ethics and dissemination:** Ethical approval is not required because this meta-  
42 analysis is based on published papers. The results of this systematic review  
43 and meta-analysis will be published in a peer-reviewed journal once we have  
44 finished this study.

**PROSPERO registration number:** CRD42020180214.

**Keywords:** novel coronavirus pneumonia, lung function, respiratory rehabilitation, physical therapy

## **Strengths and limitations of this study**

This will be the first systematic review and meta-analysis to investigate the effects of respiratory rehabilitation therapy on patients with novel coronavirus pneumonia.

To avoid errors, data extraction and bias assessment will be carried out by two reviewers independently.

Egger's test and Begg's test will be conducted to assess the publication bias with Stata 16.0 software.

Absent of sufficient randomized controlled trials may be a limitation for this meta-analysis.

## **INTRODUCTION**

In the late of December 2019, patients with viral pneumonia infected by subsequently named Coronavirus Disease 2019 (COVID-19) were reported in Wuhan, China.<sup>1</sup> COVID-19 virus has sparked a pandemic around the world and millions of people have been infected.<sup>2</sup> It is still remain difficult to manage and control COVID-19 for countries around the world.<sup>3</sup> Patients who suffered from 2019 novel coronavirus had clinical manifestations of cough, shortness of

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67 breath, chest pain and so forth.<sup>4</sup> COVID-19 is a highly contagious respiratory  
68 infection disease that can cause physical, respiratory and psychological  
69 disorders.<sup>5</sup> It is of great importance to provide the pulmonary rehabilitation  
70 methods for patients with viral pneumonia caused by COVID-19.<sup>6</sup> Respiratory  
71 rehabilitation is crucial to the recovery of patients during clinical treatment and  
72 in the rehabilitation phase.<sup>7</sup> Early rehabilitation services can improve  
73 distressing physical and psychological symptoms with lung diseases.<sup>8</sup>  
74 Previously, pulmonary rehabilitation and chest physical therapy have been  
75 proved that can provide greatest positive effects for chronic obstructive  
76 pulmonary disease (COPD) or other chronic respiratory diseases.<sup>9 10</sup> However,  
77 it is unclear whether respiratory rehabilitation therapy could improve the lung  
78 function in patients with coronavirus pneumonia. Additionally, up to now, there  
79 is no systematic review and meta-analysis which investigates the association  
80 between respiratory rehabilitation therapy and COVID-19. Therefore, we will  
81 qualitatively and quantitatively investigate the effects of respiratory  
82 rehabilitation therapy on patients with novel coronavirus in this systematic  
83 review and meta-analysis.

84

85 **METHODS**

86 **Registration**

87 This systematic review and meta-analysis protocol has been registered in the  
88 PROSPERO and the registration number is CRD42020180214. The protocol

will follow the guideline of the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA-P).<sup>11</sup>

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## 92 Patient and Public Involvement

93 No patient involved.

94

## 95 Search strategy

96 The PubMed, Embase, Web of Science, the Cochrane Central Register of  
97 Controlled Trials (CENTRAL), Chinese Biomedical Literature Database (CBM),  
98 China National Knowledge Infrastructure (CNKI), Wanfang and VIP information  
99 databases will be searched from their respective inception dates to April 15,  
100 2020. Studies about the effects of respiratory rehabilitation programs for  
101 patients with Coronavirus Disease 2019 in the rehabilitation phase will be  
102 included in this meta-analysis, including randomized controlled trials (RCTs),  
103 controlled clinical trials (CCTs), prospective and retrospective comparative  
104 cohort studies, cluster trials, cross sectional studies and observational studies.

105 The detailed information of PubMed search strategy is shown (table 1).

106

107 **Table 1** Search strategy of PubMed

Search	Query
#1	"COVID-19"[Mesh Terms]
#2	"2019 nCoV"[Title/Abstract] OR "2019nCoV"[Title/Abstract] OR "2019 novel coronavirus"[Title/Abstract] OR "COVID 19"[Title/Abstract] OR "COVID19"[Title/Abstract] OR "new coronavirus"[Title/Abstract] OR "novel coronavirus"[Title/Abstract] OR "SARS CoV-2"[Title/Abstract] OR "(Wuhan[Title/Abstract] AND coronavirus)[Title/Abstract]" OR "COVID-19"[Title/Abstract]



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OR "SARS-CoV"[Title/Abstract] OR "2019-nCoV"[Title/Abstract]  
OR "SARS-CoV-2"[Title/Abstract] OR "novel coronavirus  
pneumonia" [Title/Abstract] OR "COVID-19 pneumonia"  
[Title/Abstract]  
#3 "Respiratory rehabilitation"[Title/Abstract] OR "pulmonary  
rehabilitation"[Title/Abstract] OR "Respiratory  
therapy"[Title/Abstract] OR "pulmonary recovery"[Title/Abstract]  
OR "pulmonary rehabilitation program"[Title/Abstract] OR  
"physiotherapy"[Title/Abstract] OR "physical  
therapy"[Title/Abstract] OR "physical intervention"[Title/Abstract]  
OR "physical rehabilitation"[Title/Abstract] OR "pulmonary  
Therapy"[Title/Abstract] OR "pulmonary  
intervention"[Title/Abstract] OR "respiratory  
intervention"[Title/Abstract]  
#4 #1 OR #2  
#5 #3 AND #4

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**Eligibility criteria**

**Study design**

Relevant studies including randomized controlled trials (RCTs), controlled  
clinical trials (CCTs), prospective and retrospective comparative cohort studies,  
cluster trials, cross sectional studies and observational studies will be included  
in this meta-analysis. We attempt to search as many types of studies as  
possible because of absent original research about recently erupted COVID-  
19.

**Participants**

The patients who suffered from viral pneumonia affected by Coronavirus  
Disease 2019 and coordinated with respiratory rehabilitation treatments  
irrespective of gender and ethnicity will be involved in this meta-analysis.

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7 123 **Interventions**

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9 124 The interventions of respiratory rehabilitation therapy for viral pneumonia could  
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11 125 be breathing exercises, respiratory muscle training, chest physiotherapy or  
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13 126 other physical training programs.  
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19 128 **Outcomes**

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22 129 The outcomes will be considered in this meta-analysis are as follows: forced  
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24 130 expiratory volume in one second (FEV<sub>1</sub>), forced vital capacity (FVC), the ratio  
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26 131 of forced expiratory volume in one second and forced vital capacity (FEV<sub>1</sub>/FVC),  
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28 132 Rated Perceived Exertion (RPE) scale scores, Borg scale scores, the ratio of  
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30 133 ventilation and perfusion (V/Q), blood oxygen saturation and discharge time.  
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37 135 **Study selection and data extraction**

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39 136 **Study selection**

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42 137 Two reviewers select studies independently and any different opinions between  
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44 138 two reviewers should consult with a third reviewer to reach a consensus. We  
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46 139 will remove repetitive articles at first and then exclude irrelevant studies through  
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48 140 reading the title, abstract and the full text one by one. The study selection  
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50 141 process is demonstrated in a PRISMA flow diagram (figure 1).  
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57 143 **Data extraction**  
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A standardized form will be used to extract data by two reviewers independently and disagreements between them should be solved with the help of the third reviewer. The detailed extraction information are as follows: the first author, year of publication, country of publication, study design, sample characteristics, number of participants, experimental and control interventions, intervention time, outcomes and results.

**Quality assessment of included studies**

The Cochrane risk of bias tool with items of random sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting and other bias will be used to assess the quality of included randomized controlled trials. Otherwise, the Newcastle-Ottawa Scale (NOS) which includes consideration of patient selection, study comparability and outcome assessment will be performed to evaluate non-randomized studies quality. We need to select the suitable scale according to the type of included studies.

**Data synthesis and statistical analysis**

**Data synthesis**

Review Manager 5.3 software (Cochrane Collaboration) and Stata 16.0 software will be used to conduct this meta-analysis. Mean difference (MD) or standardized mean difference (SMD) with 95% confidence intervals (CI) is used for calculating continuous variables.

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7 167 **Assessment of heterogeneity**

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9 168 Statistical heterogeneity among included studies will be assessed by the chi-  
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12 169 square test and  $I^2$  test. We use a fixed-effect model for data analysis at first. If  
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14 170  $I^2 > 0.5$  or  $P < 0.1$ , it is considered that there is a significant heterogeneity  
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17 171 among studies and a random effects model will be used without finding suitable  
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19 172 reasons for the high heterogeneity.  
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25 174 **Subgroup analysis**

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27 175 If the heterogeneity of the included studies is large, subgroup analyses will be  
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29 176 carried out by types of respiratory rehabilitation programs.  
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35 178 **Sensitivity analysis**

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37 179 Sensitivity analysis is conducted through excluding studies one by one so that  
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39 180 we can seek out the source of heterogeneity.  
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45 182 **Assessment of publication bias**

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47 183 Egger's test and Begg's test will be conducted to assess the publication bias  
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49 184 with Stata 16.0 software.  
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55 186 **Ethics and dissemination**

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57 187 Ethical approval is not required because this meta-analysis is based on  
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published papers. The results of this systematic review and meta-analysis will  
be published in a peer-reviewed journal once we have finished this study

**DISCUSSION**

As far as we know, this is the first systematic review and meta-analysis to  
investigate the effects of respiratory rehabilitation therapy on patients with novel  
coronavirus pneumonia. Respiratory rehabilitation therapy has been widely  
applied to chronic respiratory diseases.<sup>12</sup> But, it is uncertain whether respiratory  
rehabilitation therapy could improve the lung function in patients with  
coronavirus pneumonia as a result of few original research. This is a problem  
that we and people from all over the world are worrying about. However, absent  
of sufficient randomized controlled trials may be a limitation for this meta-  
analysis.

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**Contributions**

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4 210 CW, ZM conceived and designed the study. ZF made the search strategy of  
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6 211 databases. WD, HQ, and ZC will be involved in data extraction and the  
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9 212 assessment of methodological quality. The protocol manuscripts were finished  
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12 213 by ZF. All authors have checked manuscripts and approved the publication of  
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14 214 the protocol.  
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17 215

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23  
24 218 grant number [QNRC2016376] and [Xuzhou Medical Young Talents Projects]  
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26 219 grant number [2016015].  
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## 32 221 **Competing interests statement**

35 222 None  
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## 39 224 **REFERENCES**

- 41 225 1. Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of  
42  
43 226 2019 novel coronavirus: implications for virus origins and receptor  
44  
45  
46 227 binding. *Lancet* 2020;395(10224):565-74.  
47  
48  
49 228 2. Gao Y, Yan L, Huang Y, et al. Structure of the RNA-dependent RNA  
50  
51  
52 229 polymerase from COVID-19 virus. *Science* 2020.  
53  
54  
55 230 3. Gilbert M, Pullano G, Pinotti F, et al. Preparedness and vulnerability of  
56  
57 231 African countries against importations of COVID-19: a modelling study.  
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*Lancet* 2020;395(10227):871-77.

4. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395(10223):507-13.

5. Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 2020;579(7798):270-73.

6. Yang F, Liu N, Hu JY, et al. [Pulmonary rehabilitation guidelines in the principle of 4S for patients infected with 2019 novel coronavirus (2019-nCoV)]. *Zhonghua Jie He He Hu Xi Za Zhi* 2020;43(3):180-82.

7. Working Group of Novel Coronavirus PUMCH. [Diagnosis and clinical management of 2019 novel coronavirus infection: an operational recommendation of Peking Union Medical College Hospital (V2.0)]. *Zhonghua Nei Ke Za Zhi* 2020;59(3):186-88.

8. Maddocks M, Lovell N, Booth S, et al. Palliative care and management of troublesome symptoms for people with chronic obstructive pulmonary disease. *Lancet* 2017;390(10098):988-1002.

9. Guan WJ, Zheng XY, Chung KF, et al. Impact of air pollution on the burden of chronic respiratory diseases in China: time for urgent action. *Lancet* 2016;388(10054):1939-51.

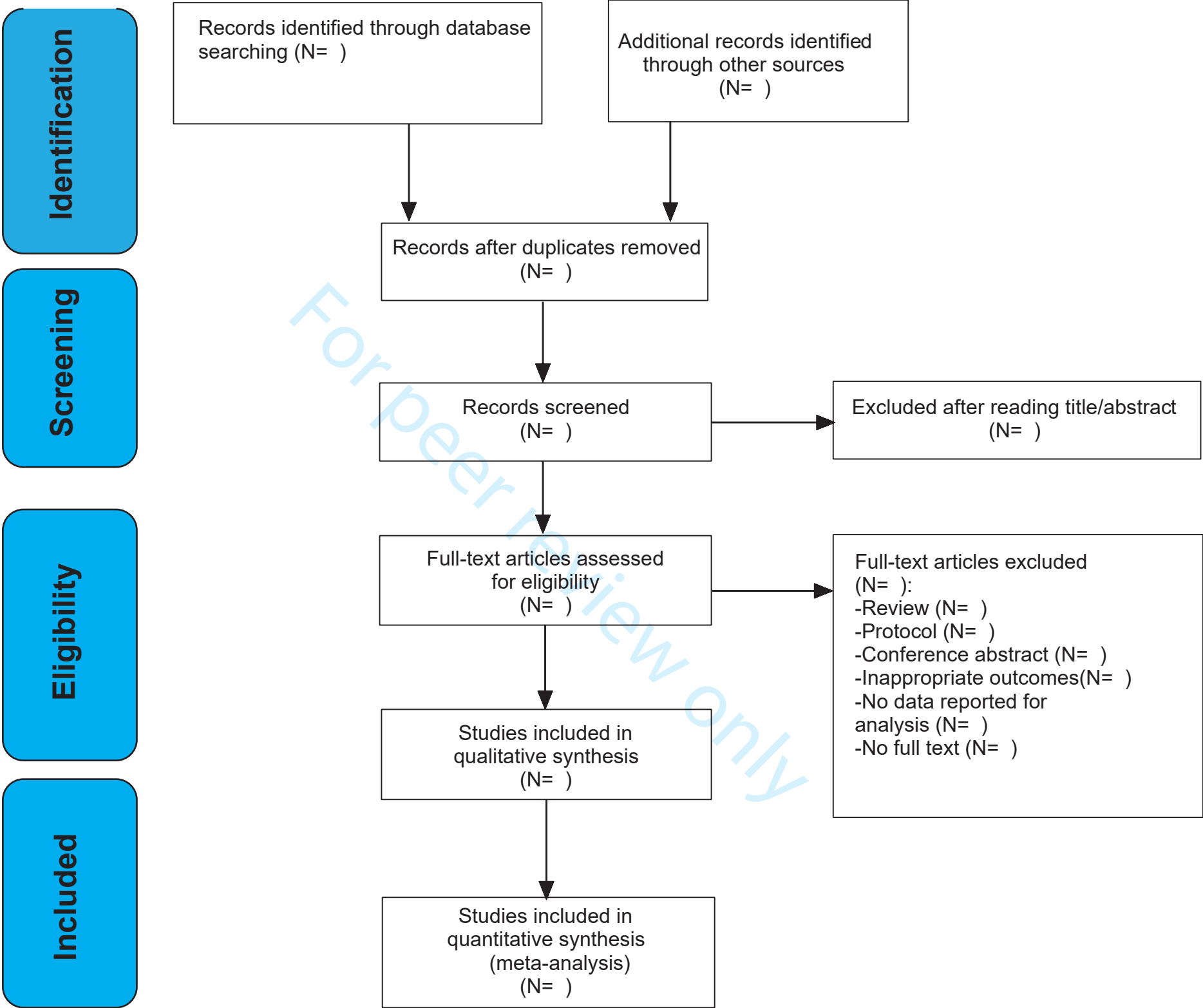
10. Spruit MA, Pitta F, McAuley E, et al. Pulmonary Rehabilitation and Physical Activity in Patients with Chronic Obstructive Pulmonary

- 254 Disease. *Am J Respir Crit Care Med* 2015;192(8):924-33.
- 255 11. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for  
256 systematic review and meta-analysis protocols (PRISMA-P) 2015  
257 statement. *Syst Rev* 2015;4:1.
- 258 12. Lacasse Y, Wong E, Guyatt GH, et al. Meta-analysis of respiratory  
259 rehabilitation in chronic obstructive pulmonary disease. *Lancet*  
260 1996;348(9035):1115-9.

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262 **Figure 1** Flow chart and descriptions of study selection. N, Number.





**Figure 1** Flow chart and descriptions of study selection. N, Number.

## PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\*

Section and topic	Item No	Checklist item
<b>ADMINISTRATIVE INFORMATION</b>		
Title:		
Identification	1a	Identify the report as a protocol of a systematic review <b>(YES)</b>
Update	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number <b>(YES, PROSPERO, CRD42020180214)</b>
Authors:		
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author <b>(YES)</b>
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review <b>(YES)</b>
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments <b>(YES)</b>
Support:		
Sources	5a	Indicate sources of financial or other support for the review <b>(YES)</b>
Sponsor	5b	Provide name for the review funder and/or sponsor <b>(YES)</b>
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol <b>(YES)</b>
<b>INTRODUCTION</b>		
Rationale	6	Describe the rationale for the review in the context of what is already known <b>(YES)</b>
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO) <b>(YES)</b>
<b>METHODS</b>		
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review <b>(YES)</b>
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage <b>(YES)</b>
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated <b>(YES)</b>
Study records:		

Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review (YES)
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis) (YES)
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators (YES)
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications (YES)
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale (YES)
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis (YES)
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised (YES)
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I <sup>2</sup> , Kendall's $\tau$ ) (YES)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression) (YES)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned (YES)
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies) (YES)
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE) (YES)

**\* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

*From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.*

# BMJ Open

## Effects of respiratory rehabilitation on patients with novel coronavirus (COVID-19) pneumonia in the rehabilitation phase: protocol for a systematic review and meta-analysis

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**Effects of respiratory rehabilitation on patients with novel coronavirus (COVID-19) pneumonia in the rehabilitation phase: protocol for a systematic review and meta-analysis**

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23     **ABSTRACT**

24     **Introduction:** The recent viral pneumonia caused by the coronavirus disease 2019  
25     (COVID-19) has gained the attention of the people all over the world. We aim to  
26     investigate the effects of respiratory rehabilitation therapy on patients infected with the  
27     novel coronavirus by conducting a systematic review and meta-analysis.

28     **Methods and analysis:** This systematic review and meta-analysis have been registered  
29     in the International Prospective Register of Systematic Reviews (PROSPERO). The  
30     PubMed, Embase, Web of Science, the Cochrane Central Register of Controlled Trials  
31     (CENTRAL), Chinese Biomedical Literature Database (CBM), China National  
32     Knowledge Infrastructure (CNKI), Wanfang Data, and VIP information databases will  
33     be searched from inception time to date without restricting research types to find  
34     relevant studies. We will also look into reference lists of relevant trials and reviews,  
35     and manually search gray literature, such as trial registries. Two reviewers will  
36     independently extract data and perform quality assessment of included studies. Review  
37     Manager 5.3 (Cochrane Collaboration) and Stata 16.0 software will be utilized to  
38     conduct this meta-analysis. The mean difference (MD) or standardized mean difference  
39     (SMD) with 95% confidence intervals (CI) is used in the computation of continuous  
40     variables to synthesize data.

41     **Ethics and dissemination:** Ethical approval is not required due to the nature of this  
42     meta-analysis, which is based on published papers. The results of this systematic review  
43     and meta-analysis will be published in a peer-reviewed journal once we finish this study.

44     **PROSPERO registration number:** CRD42020180214.

**Keywords:** COVID-19, lung function, respiratory rehabilitation, physical therapy

## **Strengths and limitations of this study**

This will be the first systematic review and meta-analysis investigating the effects of respiratory rehabilitation therapy on patients with novel coronavirus pneumonia.

To avoid errors, data extraction and bias assessment will be independently performed by two reviewers.

Egger's and Begg's tests will be conducted for the assessment of the publication bias under the use of Stata 16.0 software.

The absence of sufficient randomized controlled trials may be a limitation for this meta-analysis.

## **INTRODUCTION**

Toward the end of December 2019, patients with viral pneumonia subsequently infected by the coronavirus disease 2019 (COVID-19) were reported in Wuhan, China.<sup>1</sup>

COVID-19 has sparked a pandemic around the world, and millions of people have been infected.<sup>2</sup> The management and control of COVID-19 infection remains a challenge for countries around the world.<sup>3</sup> Patients who suffered from the 2019 novel coronavirus had clinical manifestations of cough, shortness of breath, chest pain, and so on.<sup>4</sup>

COVID-19 is a highly contagious respiratory infection disease that can cause physical, respiratory, and psychological disorders.<sup>5</sup> Pulmonary rehabilitation methods are important for patients with viral pneumonia due to by COVID-19.<sup>6</sup> Respiratory



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67 rehabilitation is crucial to the recovery of patients during clinical treatment and  
68 rehabilitation phase.<sup>7</sup> Early rehabilitation services can improve distressing physical and  
69 psychological symptoms with lung diseases.<sup>8</sup> Previously, pulmonary rehabilitation and  
70 chest physical therapy have been proven to provide the most positive effects for chronic  
71 obstructive pulmonary disease or other chronic respiratory diseases.<sup>9 10</sup> It was safe and  
72 feasible to perform early pulmonary rehabilitation in patients with acute exacerbation  
73 of lung diseases, which could effectively improve physical performance and quality of  
74 life.<sup>11 12</sup> Respiratory rehabilitation played a vital role in the non-invasive support  
75 management.<sup>13-17</sup> However, it is unclear whether respiratory rehabilitation therapy  
76 could improve lung function in patients with coronavirus pneumonia. Additionally, up  
77 to now, there is no systematic review and meta-analysis investigating the association  
78 between respiratory rehabilitation therapy and COVID-19. Therefore, we will  
79 qualitatively and quantitatively examine the effects of respiratory rehabilitation therapy  
80 on patients with novel coronavirus in this systematic review and meta-analysis.

81

82 **METHODS**

83 **Registration**

84 This systematic review and meta-analysis protocol have been registered in the  
85 International Prospective Register of Systematic Reviews (PROSPERO), and the  
86 registration number was CRD42020180214. The protocol followed the guideline of the  
87 Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA-P).<sup>18</sup>

88

## 89 Patient and Public Involvement

90 No patient involved.

91

## 92 Search strategy

93 The PubMed, Embase, Web of Science, the Cochrane Central Register of Controlled  
94 Trials (CENTRAL), Chinese Biomedical Literature Database (CBM), China National  
95 Knowledge Infrastructure (CNKI), Wanfang, and VIP information databases will be  
96 searched from inception time to date. We will also search for reference lists of relevant  
97 trials and reviews, and manually search gray literature, such as trial registries. Studies  
98 concerning the effects of respiratory rehabilitation programs for COVID-19 patients in  
99 the rehabilitation phase will be included in this meta-analysis, as well as randomized  
100 controlled trials (RCTs), controlled clinical trials (CCTs), prospective and retrospective  
101 comparative cohort studies, cluster trials, cross-sectional studies, and observational  
102 studies. The detailed information of PubMed search strategy is presented in table 1.

**Table 1** Search strategy of PubMed

Search	Query
#1	“COVID-19”[Mesh Terms]
#2	“2019 nCoV”[Title/Abstract] OR “2019nCoV”[Title/Abstract] OR “2019 novel coronavirus”[Title/Abstract] OR “COVID19”[Title/Abstract] OR “COVID 19”[Title/Abstract] OR “new coronavirus”[Title/Abstract] OR “novel coronavirus”[Title/Abstract] OR “SARS CoV-2”[Title/Abstract] OR “(Wuhan[Title/Abstract] AND coronavirus)[Title/Abstract]” OR “COVID-19”[Title/Abstract] OR “SARS-CoV”[Title/Abstract] OR “2019-nCoV”[Title/Abstract] OR “SARS-CoV-2”[Title/Abstract] OR “novel coronavirus pneumonia” [Title/Abstract] OR “COVID-19 pneumonia” [Title/Abstract] OR “corona-virus*”[Title/Abstract] OR “coronavirus*”[Title/Abstract] OR “NcovWuhan*”[Title/Abstract] OR “NcovHubei*”[Title/Abstract] OR “NcovChina*”[Title/Abstract] OR “NcovChinese*”[Title/Abstract]

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#3                    “Respiratory rehabilitation”[Title/Abstract] OR “pulmonary  
rehabilitation”[Title/Abstract] OR “Respiratory therapy”[Title/Abstract]  
OR “pulmonary recovery”[Title/Abstract] OR “pulmonary  
rehabilitation program”[Title/Abstract] OR  
“physiotherapy”[Title/Abstract] OR “physical therapy”[Title/Abstract]  
OR “physical intervention”[Title/Abstract] OR “physical  
rehabilitation”[Title/Abstract] OR “pulmonary Therapy”[Title/Abstract]  
OR “pulmonary intervention”[Title/Abstract] OR “respiratory  
intervention”[Title/Abstract] OR “breath\*”[Title/Abstract] OR  
“exercis\*”[Title/Abstract] OR “train\*”[Title/Abstract] OR “fitness\*”  
[Title/Abstract] OR “aerobic”[Title/Abstract] OR “resistanc\*”  
[Title/Abstract] OR “endurance”[Title/Abstract] OR “inspiratory  
muscle train\*”[Title/Abstract] OR “inspiratory muscle strength”  
[Title/Abstract] OR “respiratory muscle train\*”[Title/Abstract] OR  
“respiratory muscle strength”[Title/Abstract] OR “respiratory muscle  
endurance” [Title/Abstract] OR “muscle relaxation therapy”  
[Title/Abstract] OR “hydrotherapy” [Title/Abstract] OR “swim\*”  
[Title/Abstract] OR “bik\*”[Title/Abstract] OR “joy\*”[Title/Abstract]  
OR “walk\*”[Title/Abstract] OR “run\*”[Title/Abstract] OR “danc\*”  
[Title/Abstract] OR “sport\*”[Title/Abstract] OR “active circular  
breathing technique”[Title/Abstract] OR “ACBT” [Title/Abstract] OR  
“chest expansion”[Title/Abstract] OR “forced exhalation  
technique”[Title/Abstract] OR “airway clearance”[Title/Abstract] OR  
“mechanical cough assist” [Title/Abstract] OR “manual  
technique”[Title/Abstract] OR “mechanical device”[Title/Abstract] OR  
“positive expiratory pressure”[Title/Abstract] OR “power  
breath”[Title/Abstract]

#4                    #1 OR #2

#5                    #3 AND #4

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- 105
- 106    **Eligibility criteria**
- 107    **Study design**
- 108    Relevant studies, including randomized controlled trials (RCTs), controlled clinical
- 109    trials (CCTs), prospective and retrospective comparative cohort studies, cluster trials,
- 110    cross-sectional studies, and observational studies will be included in this meta-analysis.
- 111    We attempt to search as many types of studies as possible due to the absence of original

112 research on the recently emerging COVID-19.

113

#### 114 **Participants**

115 Patients who suffered from viral pneumonia caused by the coronavirus disease 2019  
116 and coordinated with respiratory rehabilitation treatments regardless of section,  
117 whether in the intensive care unit (ICU), intermediate respiratory unit, general ward, or  
118 rehabilitation facility will be involved in this meta-analysis. There will be no  
119 restrictions with respect to gender, age, or ethnicity.

120

#### 121 **Interventions**

122 The interventions of respiratory rehabilitation therapy for viral pneumonia could be  
123 breathing exercises, respiratory muscle training, chest physiotherapy, active circular  
124 breathing technique, chest expansion exercises, forced exhalation technique, airway  
125 clearance techniques, positive expiratory pressure, using mechanical devices (e.g.  
126 mechanical cough assist), exercise training (aerobic exercise or, resistance and  
127 endurance training), or other physical training programs.

128

#### 129 **Outcomes**

130 The primary outcomes of interest will be 6-minute walking distance (6MWD),  
131 cardiopulmonary exercise test (CPET), quality of life. The secondary outcomes are as  
132 follows: body mass index, arterial partial pressure of oxygen/fraction of inspired  
133 oxygen (PaO<sub>2</sub>/FiO<sub>2</sub>) ratio, forced expiratory volume in one second (FEV<sub>1</sub>), forced vital

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capacity (FVC), ratio of forced expiratory volume in one second and forced vital capacity (FEV1/FVC), baseline dyspnea index (BDI), rating of perceived exertion scale scores, Borg scale scores, blood oxygen saturation, and discharge time.

**Study selection and data extraction**

**Study selection**

Two reviewers independently select studies, and any disagreement between the two reviewers should be consulted by a third reviewer to reach a consensus. We will remove repetitive articles at first and exclude irrelevant studies based on the title, abstract, and the full text. The study selection process is demonstrated in a PRISMA flow diagram (figure 1).

**Data extraction**

A standardized form will be used by two reviewers to extract data independently, and disagreements between them should be solved with the help of a third reviewer. The detailed extraction information are as follows: the first author, year of publication, country of publication, study design, sample characteristics, number of participants, experimental and control interventions, intervention time, outcomes, and results. We will try our best to contact the corresponding authors of the studies through email to deal with missing data.

**Quality assessment of included studies**

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4 156 The Cochrane risk of bias tool with items of random sequence generation, allocation  
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6 157 concealment, blinding, incomplete outcome data, selective reporting, and other biases  
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9 158 will be used to assess the quality of included randomized controlled trials. Otherwise,  
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12 159 the Newcastle-Ottawa Scale, which includes consideration of patient selection, study  
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14 160 comparability, and outcome assessment will be used to evaluate the quality of non-  
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17 161 randomized studies. We need to select a suitable scale according to the types of studies  
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## 25 164 **Data synthesis and statistical analysis**

### 26 27 165 **Data synthesis**

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30 166 Review Manager 5.3 (Cochrane Collaboration) and Stata 16.0 software will be used to  
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32 167 conduct this meta-analysis. The mean difference (MD) or standardized mean difference  
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35 168 (SMD) with 95% confidence intervals (CI) is used to calculate continuous variables.  
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### 40 170 **Assessment of heterogeneity**

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43 171 Statistical heterogeneity among included studies will be assessed using the chi-squared  
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45 172 test and  $I^2$  test. We use a fixed-effect model for data analysis at first. If  $I^2 > 0.5$  or  $P <$   
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48 173  $0.1$ , it is considered that there is a significant heterogeneity among the studies, and  
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51 174 random-effect model will be used without examining the probable cause for the high  
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53 175 heterogeneity.<sup>19</sup>  
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### 58 177 **Subgroup analysis**

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If there is a large heterogeneity in the included studies, subgroup analyses will be performed on different types of respiratory rehabilitation programs and in different treatment locations, such as, intensive care unit (ICU), intermediate respiratory unit, general ward, or rehabilitation facility.

**Sensitivity analysis**

Sensitivity analysis is conducted by excluding studies one by one, so that we can determine the source of heterogeneity.

**Assessment of publication bias**

Publication bias will be examined according to the funnel plot method. Also, Egger’s test and Begg’s test will be conducted to quantitatively assess the publication bias using the Stata 16.0 software.

**Quality of evidence**

We will use the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) guidelines for the assessment of the strength of evidence for each outcome. The result will be categorized as high, moderate, low, and very low certainty of evidence.<sup>20</sup>

**Ethics and dissemination**

Ethical approval is not required due to the nature of this meta-analysis, which is based

on published papers. The results of this systematic review and meta-analysis will be published in a peer-reviewed journal once we finish this study.

202

## 203 **DISCUSSION**

204 To the best of our knowledge, this is the first systematic review and meta-analysis to  
205 investigate the effects of respiratory rehabilitation therapy on patients with novel  
206 coronavirus pneumonia. Respiratory rehabilitation therapy has been widely applied to  
207 patients with chronic respiratory diseases.<sup>21</sup> However, it is uncertain whether  
208 respiratory rehabilitation therapy could improve lung function in patients with  
209 coronavirus pneumonia due to limited original research. This is a major concern for us  
210 and for everyone around the world. Nonetheless, the lack of sufficient randomized  
211 controlled trials may be a limitation for this meta-analysis.

212

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## 221 **Acknowledgements**



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**Contributions**

CW, ZM conceived and designed the study. ZF made the search strategy of databases. WD, HQ, GM, and ZC will be involved in data extraction and the assessment of methodological quality. The protocol manuscripts were finished by ZF. All authors have checked manuscripts and approved the publication of the protocol.

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**Competing interests statement**

None declared.

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245 **REFERENCES**

- 246 1. Lu R, Zhao X, Li J, *et al.* Genomic characterisation and epidemiology of 2019  
247 novel coronavirus: implications for virus origins and receptor binding. *Lancet*  
248 2020;395(10224):565-74.
- 249 2. Gao Y, Yan L, Huang Y, *et al.* Structure of the RNA-dependent RNA  
250 polymerase from COVID-19 virus. *Science* 2020.
- 251 3. Gilbert M, Pullano G, Pinotti F, *et al.* Preparedness and vulnerability of African  
252 countries against importations of COVID-19: a modelling study. *Lancet*  
253 2020;395(10227):871-77.
- 254 4. Chen N, Zhou M, Dong X, *et al.* Epidemiological and clinical characteristics of  
255 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive  
256 study. *Lancet* 2020;395(10223):507-13.
- 257 5. Zhou P, Yang XL, Wang XG, *et al.* A pneumonia outbreak associated with a  
258 new coronavirus of probable bat origin. *Nature* 2020;579(7798):270-73.
- 259 6. Yang F, Liu N, Hu JY, *et al.* [Pulmonary rehabilitation guidelines in the principle  
260 of 4S for patients infected with 2019 novel coronavirus (2019-nCoV)].  
261 *Zhonghua Jie He He Hu Xi Za Zhi* 2020;43(3):180-82.
- 262 7. Working Group of Novel Coronavirus PUMCH. [Diagnosis and clinical  
263 management of 2019 novel coronavirus infection: an operational  
264 recommendation of Peking Union Medical College Hospital (V2.0)]. *Zhonghua*  
265 *Nei Ke Za Zhi* 2020;59(3):186-88.

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8. Maddocks M, Lovell N, Booth S, *et al.* Palliative care and management of troublesome symptoms for people with chronic obstructive pulmonary disease. *Lancet* 2017;390(10098):988-1002.

9. Guan WJ, Zheng XY, Chung KF, *et al.* Impact of air pollution on the burden of chronic respiratory diseases in China: time for urgent action. *Lancet* 2016;388(10054):1939-51.

10. Spruit MA, Pitta F, McAuley E, *et al.* Pulmonary Rehabilitation and Physical Activity in Patients with Chronic Obstructive Pulmonary Disease. *Am J Respir Crit Care Med* 2015;192(8):924-33.

11. He M, Yu S, Wang L, *et al.* Efficiency and safety of pulmonary rehabilitation in acute exacerbation of chronic obstructive pulmonary disease. *Med Sci Monit* 2015;21:806-12.

12. Hoffman M, Chaves G, Ribeiro-Samora GA, *et al.* Effects of pulmonary rehabilitation in lung transplant candidates: a systematic review. *BMJ Open* 2017;7(2):e013445.

13. Lazzeri M, Lanza A, Bellini R, *et al.* Respiratory physiotherapy in patients with COVID-19 infection in acute setting: a Position Paper of the Italian Association of Respiratory Physiotherapists (ARIR). *Monaldi Arch Chest Dis* 2020;90(1).

14. Cilione C, Lorenzi C, Dell Orso D, *et al.* Predictors of change in exercise capacity after comprehensive COPD inpatient rehabilitation. *Med Sci Monit* 2002;8(11):CR740-5.

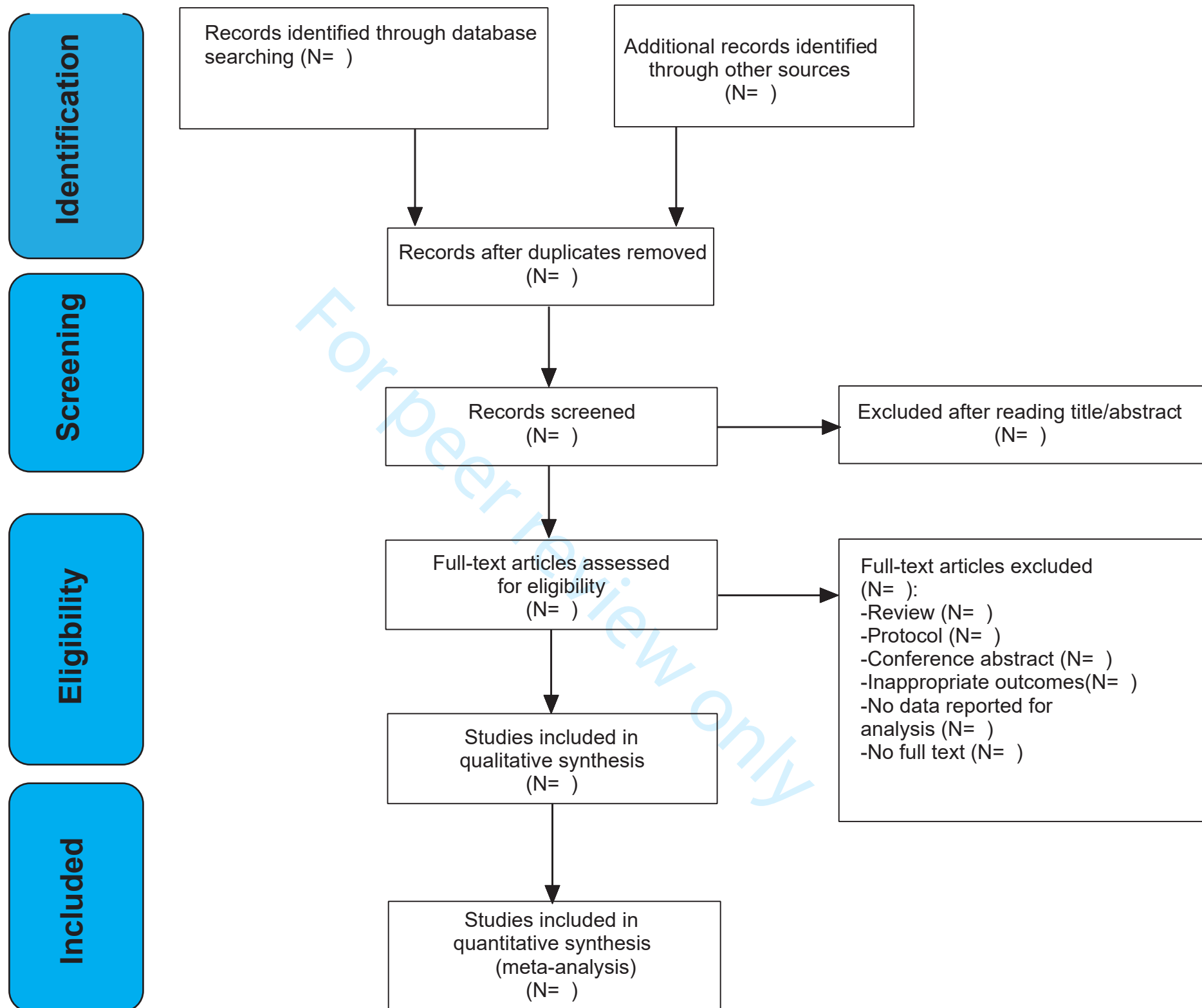
15. Paneroni M, Simonelli C, Saleri M, *et al.* Short-Term Effects of Normocapnic

- Hyperpnea and Exercise Training in Patients With Chronic Obstructive Pulmonary Disease: A Pilot Study. *Am J Phys Med Rehabil* 2018;97(12):866-72.
16. Paneroni M, Simonelli C, Vitacca M, *et al.* Aerobic Exercise Training in Very Severe Chronic Obstructive Pulmonary Disease: A Systematic Review and Meta-Analysis. *Am J Phys Med Rehabil* 2017;96(8):541-48.
17. Vitacca M, Kaymaz D, Lanini B, *et al.* Non-invasive ventilation during cycle exercise training in patients with chronic respiratory failure on long-term ventilatory support: A randomized controlled trial. *Respirology* 2018;23(2):182-89.
18. Moher D, Shamseer L, Clarke M, *et al.* Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4:1.
19. Moher D, Liberati A, Tetzlaff J, *et al.* Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med* 2009;6(7):e1000097.
20. Guyatt G, Oxman AD, Akl EA, *et al.* GRADE guidelines: Introduction—GRADE evidence profiles and summary of findings tables. *Journal of clinical epidemiology* 2011;64(4):383-94.
21. Lacasse Y, Wong E, Guyatt GH, *et al.* Meta-analysis of respiratory rehabilitation in chronic obstructive pulmonary disease. *Lancet* 1996;348(9035):1115-9.

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- 310     **Table 1**    Search strategy of PubMed
- 311     **Figure 1**    Flow chart and descriptions of study selection. N, Number.

For peer review only



**Figure 1** Flow chart and descriptions of study selection. N, Number.

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**PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\***

Section and topic	Item No	Checklist item
<b>ADMINISTRATIVE INFORMATION</b>		
Title:		
Identification	1a	Identify the report as a protocol of a systematic review <b>(YES)</b>
Update	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number <b>(YES, PROSPERO, CRD42020180214)</b>
Authors:		
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author <b>(YES)</b>
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review <b>(YES)</b>
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments <b>(YES)</b>
Support:		
Sources	5a	Indicate sources of financial or other support for the review <b>(YES)</b>
Sponsor	5b	Provide name for the review funder and/or sponsor <b>(YES)</b>
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol <b>(YES)</b>
<b>INTRODUCTION</b>		
Rationale	6	Describe the rationale for the review in the context of what is already known <b>(YES)</b>
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO) <b>(YES)</b>
<b>METHODS</b>		
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review <b>(YES)</b>
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage <b>(YES)</b>
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated <b>(YES)</b>
Study records:		

Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review <b>(YES)</b>
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis) <b>(YES)</b>
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators <b>(YES)</b>
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications <b>(YES)</b>
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale <b>(YES)</b>
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis <b>(YES)</b>
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised <b>(YES)</b>
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as $I^2$ , Kendall's $\tau$ ) <b>(YES)</b>
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression) <b>(YES)</b>
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned <b>(YES)</b>
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies) <b>(YES)</b>
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE) <b>(YES)</b>

**\* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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